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EXAMINER	
ROYDS, LESLIE A	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/083,283	DUGAN ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2006 and 13 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-12 and 70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-12 and 70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/26/06&7/19/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-12 and 70 are presented for examination.

Applicant's Amendments filed June 26, 2006 and July 13, 2006 have each been received and entered into the present application. Applicant's Information Disclosure Statements (IDS) filed June 26, 2006 (three pages) and July 19, 2006 (two pages) have each been received and entered into the application. As reflected by the attached, completed copies of form PTO/SB/08A (five pages total), the Examiner has considered the cited references.

Claims 1, 3-12 and 70 remain pending and are under examination. Claim 15 has been cancelled and claims 1 and 70 are amended.

Applicant's arguments, filed June 26, 2006 and July 13, 2006, have been fully considered but they are not deemed to be persuasive. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 112, Written Description Requirement

(New Grounds of Rejection)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-12 and 70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Present claim 1 is directed to a process for extending the lifespan of a mouse, human or a cell thereof beyond a generic expected lifespan for said mouse, said human or said cell thereof comprising the administration to said mouse, human or cell thereof a therapeutically effective amount of a composition comprising a C60 compound or a combination of such C60 compounds selected from the group consisting of *e,e,e,* C60(C(COOH)2)2(CHCOOH); *e,e,e* C60(CHCOOH))3; C60(C(COOH)2)n (where n=1, 2, or 3), and pharmaceutically acceptable salts, esters or amides thereof.

In particular, Applicant has failed to (1) provide adequate written support to now claim "or a cell thereof" as it refers to mouse or human and (2) provide adequate written support for the genus of pharmaceutically acceptable esters or amides of those C60 compounds presently claimed.

Regarding Applicant's newly added limitation directed to "a mouse, a human or a cell thereof", Applicant fails to direct the Examiner to a specific portion of the specification that provides adequate written support to now claim "or a cell" of a mouse or human. In essence, such amounts to the extension of lifespan of a mouse cell or a human cell *in vitro*. However, the only disclosure present in the specification or claims as originally filed refers to both a metazoan or metazoan cells or a mammal. Please see the claims as originally filed and also the specification at page 1, Section 1 and also, for example, at page 16, second paragraph. The specification does not, however, disclose this process for use in, particularly, a cell of a mouse or human.

The disclosure of "metazoan or metazoan cells" or "mammal" in general does not provide sufficient written basis to now claim the execution of the same process as substantially claimed for use in a cell of a mouse or a cell of a human. Such circumstances amount to *in vitro* circumstances using mouse cell(s) or human cell(s), which is a narrowing of the subject matter originally disclosed in the specification and claims as originally filed. Additionally, the examples provided in the specification as originally filed are directed to *in vivo* studies, so the implicit suggestion of the concept of "or a cell thereof" as it relates to a cell of a mouse or human is not provided in the disclosure as originally filed.

Regarding the requirement for adequate written description of the pharmaceutically acceptable esters or amides presently claimed, Applicant's attention is directed to the MPEP at §2163. In particular, *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089, 118 S. Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plan for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for *Examination of Patent Applications* under the 35 U.S.C. 112.1 "Written Description" Requirement ("*Guidelines*"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics when coupled with a known or disclosed correlation between function and structure..." *Enzo Biochem v. Gen-Probe Inc.*, 296 F.3d 316, 1324-25 (Fed. Cir. 2002) (quoting *Guidelines*, 66 Fed. Reg. at 1106 (emphasis added)). Moreover, although *Eli Lilly* and *Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. *Univ. of Rochester v. G.D. Searle & Co.*, 249 Supp. 2d 216, 225 (W.D.N.Y. 2003).

Present claim 1 is directed to pharmaceutically acceptable esters or amides of the C60 compounds expressly recited in the claim [i.e., *e,e,e,* C60(C(COOH)2)2(CHCOOH); *e,e,e* C60(CHCOOH))3; C60(C(COOH)2)n (where n=1,2 or 3)]. However, Applicant has failed to provide sufficient written description to support the use of a pharmaceutically acceptable ester or amide thereof. In fact, the present disclosure fails to recite any structural characteristics, chemical formula, name(s) or physical properties that would provide adequate description of the pharmaceutically acceptable esters or amides that Applicant was actually in possession of, and intended to be used within the context of the present invention, at the time of the present invention. The specification fails to contain any limiting definition or

any structural, chemical or physical characteristics of these esters or amides such that one of ordinary skill in the art would have been able to readily identify the scope of those compounds encompassed by the terms "pharmaceutically acceptable esters or amides thereof". Additionally, there is no direction as to what degree of derivation a compound may have from the parent C60 compounds recited in the claims and still be considered an "ester" or "amide" as intended by Applicant.

Considering the teachings provided in the specification as originally filed, Applicant has failed to provide the necessary teachings, by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams and formula that fully set forth the claimed invention, in such a way as to reasonably convey to one skilled in the relevant art that Applicant had possession of the concept of (1) extending the lifespan of a cell of a mouse of human or (2) the genus of pharmaceutically acceptable esters or amides of the C60 compounds *e,e,e,* C60(C(COOH)2)2(CHCOOH); *e,e,e* C60(CHCOOH))3; C60(C(COOH)2)n (where n=1, 2, or 3).

Accordingly, for these reasons, claims 1, 3-12 and 70 are properly rejected under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement.

Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-12 and 70 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for extending the lifespan of mice comprising the administration of the C60 compound *e,e,e,* C60(C(COOH)2)2(CHCOOH); *e,e,e* C60(CHCOOH))3; C60(C(COOH)2)n and pharmaceutically acceptable salts thereof, does not reasonably provide enablement for the extending the lifespan of a human comprising the administration of the same, for the reasons of record set forth at pages

3-18 of the previous Office Action dated January 25, 2006, of which said reasons are herein incorporated by reference.

Applicant's remarks have been fully considered in their entirety, but fail to be persuasive as they relate to the concept of extrapolating the longevity extending results demonstrated in the C57B6NIH caloric restricted mice of Example 2 to humans.

Applicant references the Roth et al. publication as evidence that mice are the most widely accepted model for the study of aging with potential relevance to human aging and age-related disease. Applicant further states that, "The question at hand however is not what model theoretically is the most predictive, but rather what models were recognized in the art as having predictive value. What this statement makes clear is that models such as rodents and even invertebrates are viewed by those skilled in the art as having predictive value." (see page 7 of Applicant's remarks)

It appears, however, that Applicant has taken the statements of Roth et al. out of context and is attributing a conclusion to the statements made in Roth et al. that is not expressly, nor implicitly, suggested by the reference. For example, Roth et al. notes that rodents are widely used as animal models for gerontology and that studies in invertebrates have provided some insight into the *aging process*. However, such statements do not equate to the conclusion that rodents are recognized in the art as reasonably predictive of the same or substantially similar level of efficacy in humans or that invertebrates are predictive of human efficacy. In fact, Roth et al. expressly states to the contrary by stating, "*Given the complexity of human physiology, however, models more phylogenetically similar to humans are needed.*" This clearly and unequivocally indicates that animal models with a higher degree of phylogenetic similarity are needed in the art to provide greater predictive relevance to a human model. In other words, the state of the art is actually inviting further research and exploration into animal models to discover models with greater genetic relevance to humans such that extrapolation of the results from the animal model to a human would logically follow.

Applicant further relies upon Pugh et al. in support of their assertion that mice have been used to study potential life-extending treatments in humans. Applicant states that Pugh et al. selected to study DHEAS supplementation "because of extensive current human usage in the face of limited data to support the benefits of this practice." (see page 7 of Applicant's remarks) Applicant further submits that Pugh et al. determined that DHEAS supplementation had no significant effect on the lifespan of mice, which was consistent with their observation that there is limited data supporting any effect in humans.

In response thereto, Applicant appears to be confusing the phrase "limited data" with a lack of lifespan extending effect from DHEAS supplementation and then draws the conclusion that the experiment of Pugh et al. failed to show a lifespan-extending effect in mice, which was a result consistent with the "limited data" of DHEA supplementation in humans. However, Applicant is referred to the abstract, which states, "Dietary manipulations to prevent cancer and other diseases of aging have drawn broad public and scientific attention. One indicator of this interest is that dehydroepiandrosterone (DHEA) supplements are widely consumed by those who hope that this hormone may keep them 'younger longer'. *However, key data to support this belief are lacking. For example, the influence of DHEA treatment on spontaneous cancer and lifespan in healthy, long-lived strains of mice or rats is unknown. This is in contrast to the situation for caloric restriction (CR), which is known to oppose cancer development and increase maximum lifespan in rodents."* (emphasis added) It is clear from this discussion that Pugh et al. intends the phrase "limited data" to mean that there is a *lack* of data in the art demonstrating the efficacy of DHEAS in extending lifespan in healthy mice or humans. A lack of data most certainly does not equate to a negative effect. In fact, it is impossible to allege a result from the art when no data exists to support such a conclusion. Thus, Applicant's assertion that the lack of efficacy in mice is consistent with the lack of efficacy in humans is not persuasive because Pugh et al. expressly states that there is a *lack of data in the art with regard to the lifespan extending effects of DHEAS supplementation in humans.*

Regarding Applicant's response to the citation of *Ex parte Maas*, Applicant states, "In *Maas*, the Examiner analyzed a "defect in experimental design" of the in vivo studies described (the Board did not provide details of this defect). *Maas*, 9 USPQ2d at 1748. In the present case, however, the Examiner has not identified any defects in experimental design that would question the truthfulness of Applicant's assertions." (see page 9 of Applicant's remarks)

In response thereto, the Examiner cites Kuro-o, "Disease Model: Human Aging" (*Trends in Molecular Medicine*, April 2001). Kuro-o states, "Very little is known about the molecular mechanism of human aging. This, at least in part, derives from a paucity of appropriate animal models of aging. Until recently, the senescence-accelerated mouse was the only mammalian model of aging. However, novel mouse models that exhibit multiple aging phenotypes have been developed in the past few years by disruption of the klotho gene, the telomerase gene and the genes involved in premature aging syndromes. These mouse models are expected to be important tools for aging research." (see abstract) Applicant is directed to the Table at page 180. Kuro-o further states, "Aging is a complex biological phenomenon in which multiple genetic and environmental components are involved. Aging in vivo arises because of the contribution of different pathways acting at various levels. Therefore, it is very unlikely that only a single gene mutation in mice recapitulates all the characteristic features of human aging. In fact, none of the animal models displays all phenotypes of aging. In addition, although their phenotypes are very similar to those of natural aging, the mechanism by which they develop aging might not be identical to that of natural aging." (see column 2, last paragraph, page 181)

Kuro-o expressly acknowledges the unpredictability in the art with regard to animal models of aging and further suggests that those models disclosed in the publication were the only animals models possibly suggestive of predictive human efficacy. However, Applicant's experiment upon which he relies as enabling support of lifespan extension in both mice and humans was performed in a C57B6 mouse, which is not one of the models recognized by Kuro-o as a potentially predictive animal model.

As referenced by Applicant, the MPEP states at §2164.02, "[I]f the art is such that a particular model is recognized as correlating to a specific condition, *then it should be accepted as correlating unless the Examiner has evidence that the model does not correlate." In re Brana*, 51 F.3d 1560, 1566 (Fed. Cir. 1995) (emphasis added) It is clear that there is no evidence presented on the record or in the art that the particular mouse strain used in Applicant's experiment was suggested to have predictive human efficacy or even that it was recognized in the art as a possible model for predictive efficacy in human aging. The Examiner relies upon the teachings of Kuro-o in support of this conclusion. Therefore, and in accordance with *In re Brana*, Applicant's mouse model is not accepted as correlating to human efficacy because the art specifically teaches away from such a conclusion.

Applicant is further reminded that a conclusion of a lack of enablement must take into consideration the unpredictability in the art at the time of the invention and the direction or guidance provided by Applicant. The amount of guidance required to be present in the specification as originally filed is directly proportional to the amount of knowledge in the art as well as the unpredictability in the art. In other words, if little or nothing is known in the prior art about an aspect of the claimed invention and the art is unpredictable, the specification needs more detail and guidance as to how to use the invention in order to be enabling. Please reference *In re Fisher*, 417 F.2d 833, 839, 166 USPQ 18, 23 (CCPA 1970) and *Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004). In other words, the fact that the art recognized the unpredictability of animal models, particularly mice, of human aging is further evidence that the specification must contain more detail and guidance as to how to use the present invention in humans such that the skilled artisan would have been imbued with at least a reasonable expectation of success in achieving the lifespan extending effect as claimed without requiring an undue level of experimentation to determine how the results show in the C57B6 mice were suggestive of the same level of efficacy in humans.

Applicant's assertions that calorie restriction is a life extending process that can occur across

diverse species and has been shown to have similar effects in mice and in humans (see pages 11-13 of Applicant's remarks) have been considered but fail to be persuasive because calorie restriction is distinctly different process than the method substantially claimed in the present application. Calorie restriction can also be executed relatively simply and with minimal complexity, since the only requirement is that the total daily intake of calories is decreased. However, the presently claimed method is significantly more complex and requires the consideration of many factors, including, but nor limited to, the determination of the dosage amounts needed, the frequency of administration, toxicological effects, pharmacological and pharmacokinetic effects and the duration of administration. In other words, there are a number of considerations that must be taken into account in the presently claimed method that are not required for calorie restriction that preclude the assumption that just because calorie restriction is a method of extending lifespan across several different species that the same must be true for a method significantly more intricate and complex that calorie restriction *per se*. Furthermore, though Applicant makes the tenuous correlation of calorie restriction and the administration of carboxyfullerenes as methods with a similar mechanism of action (i.e., antioxidative activity), it is again noted that natural dietary modifications do not lend themselves to being suggestive or predictive of the activity of carboxyfullerene compounds in extending lifespan because there are significant chemical, functional and structural interactions that would be unique to the presently claimed carboxyfullerene compounds that would affect their activity in extending lifespan, which are considerations that are not present in merely modifying the diet.

Applicant further relies upon the decisions of *Cross* and *Brana* and states that, "The Federal Circuit has held in *Cross* and *Brana* that the enablement requirement of 35 U.S.C. 112 for claims directed to asserted therapeutic uses is satisfied in cases where compounds were only tested in vivo or model in vivo systems (i.e., mice): Usefulness in patent laws, and in particular in the context of pharmaceutical inventions, *necessarily includes the expectation of further research and development.* The stage at which

an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer. In view of all the foregoing, we conclude that Applicants' disclosure complies with the requirements of U.S.C. 112, first paragraph. *In re Brana*, 51 F.3d 1560."

First, it is noted that each case before the Patent Office is decided on its own merits and in preponderance of the evidence, amendments and arguments presented in each unique case. Decisions made in previous cases before the Office or to the higher courts are not necessarily binding to the course of prosecution. Therefore, Applicant's reliance upon *Cross* and *Brana* in support of their assertion that the mouse model presented herein is sufficient to satisfy the enabling requirement of 35 U.S.C. 112, first paragraph, has been considered, but is not persuasive. Each of these cases involved distinctly different fact patterns from the present case and, therefore, cannot be relied upon to direct the decisions made during prosecution of the present application.

Regardless, however, while it is acknowledged that Applicants for patent are not required to reduce the invention directly to practice in a human model in order to claim the use of the therapy in humans, nor are they required to progress to Phase II clinical trials involving human subjects, evidence or soundly scientific reasoning must be provided as to why one of ordinary skill in the art would have expected the in vivo animal results to be suggestive of the same or substantially similar efficacy in humans when the art clearly dictates to the contrary. It is not enough to rely upon presumption. Where the state of the art is sufficiently unpredictable that the skilled artisan would not have reasonably expected such results to be achieved across species lines, a person having ordinary skill in the art would have been skeptical to extrapolate the results presently shown in mice to humans in general in the absence of any concrete evidence on this record stating the definitive correlation between the C57B6 mice and humans.

In the absence of such evidence, the skilled artisan would have no alternative recourse but undue experimentation.

Regarding the arguments directed to the experimental controls, Applicant states, "With respect to the effect of feeding, it is art accepted practice in studies of aging to state whether animals or humans have been subjected to caloric restriction when reporting such data. Applicants did not report any caloric restrictions as none were imposed. Nonetheless, Applicants establish for the record that both the treated and untreated mice of the experiment reported in Figure 4 of this application were fed ad libitum. Consequently, the longevity effect observed can be attributed to the C60 fullerene administration rather than to some combination of dietary and compound-mediated effects as postulated by the examiner. Given that the treated mice did not exhibit any decrease in weight relative to the control mice (Specification Page 22, line 2-3), there is no reason to believe that the treated mice were somehow preferentially subjected to any caloric restrictions that could have accounted for the observed effects on longevity." (see paragraph bridging pages 17-18 of Applicant's remarks)

In response thereto, Applicant's attention is directed to the "Available Strains" from the National Institute of Aging (www.nia.nih.gov). In particular, it is noted that the C57BL/6 available from the National Institute of Aging is, in fact, contrary to Applicant's assertions, a calorie restricted mouse strain. As previously noted by the Examiner in the prior Office Action at pages 16-17, "Calorie restriction was a process well known in the art as a method of inhibiting the aging process and thereby extending lifespan in this animal. In this regard, Brack et al. (EMBO Workshop Report: Molecular and Cellular Gerontology, 1999) is cited. 'Calorie restriction is one of the few regimes that positively influences most aspects of aging in all organisms tested so far. Brian Merry (Liverpool, UK) reported on the positive effect calorie restriction has on the lifespan of rodents, Rhesus monkeys and squirrel monkeys. In rats, calorie restriction alters the rate of aging, resulting in life extension. When these calorie-restricted animals are refed normal diet, aging is again accelerated.' (see Brack et al., middle paragraph at column 1,

page 1932)." Therefore, in light of the fact that, absent factual evidence to the contrary, the mouse strain used by Applicant is a calorie restricted strain, Applicant would need to show what portion of the extended survival effect would have been attributable to the diet alone and what portion would have been attributable to the fullerene compound alone.

Lastly, in response to the issue raised as to whether the studied mice had any other genetic mutations that may have contributed to or retarded against increased lifespan in the mice, Applicant states, "All of the mice used in Applicants' longevity studies were of the same inbred genetic strain...Moreover, the specification further reveals that the inbred strain of mice were obtained from the National Institute of Aging mouse colonies, so it is very difficult to imagine a scenario where the treated population was somehow comprised of mutant mice as the Examiner posits. In fact, the present of any dwarf mice in the treated population would have been obvious and presumably been reflected in a reduction in weight of the treated mice." (see page 18 of Applicant's remarks)

In response thereto, it is noted that the fact that the strain used in Applicant's experiment was inbred does not preclude the existence of other, possibly silent, genetic mutations in the mice. In fact, the only requirement of the mice is that they carry the C57B6 mutation, but, again, does not preclude the presence of other genetic mutations. Applicant presumes that there were no other genetic mutations because there were no dwarf mice in the population. However, such evidence cannot be relied upon to demonstrate that none of the mice carried any additional genetic mutations because the weight of each mouse is expected to vary, so it would be impossible to definitively determine, in the absence of any genetic testing to determine the genetic makeup of each mouse, whether there were any other genetic mutations in the mice that would contribute to the lifespan extending effect of the claimed compounds. Respectfully, Applicant's presumption in the absence of any definitive genetic testing of the studied mice is insufficient to establish that additional genetic mutations were not present.

While a lack of a working embodiment in humans cannot be the sole factor in determining

enablement, the absence of evidence commensurate in scope with the presently claimed subject matter, in light of the unpredictable nature of the art and the direction that Applicant has presented, provides additional weight to the present conclusion of insufficient enablement in consideration of the *Wands* factors as a whole. The basis for the present rejection is not simply that experimentation would be required, since it is clear from the state of the prior art and Applicant's disclosure and remarks that experimentation in this particular art is not at all uncommon, but that the experimentation required in order to practice this aspect of the invention would be *undue*. Please reference *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976), which states, "The test of enablement is not whether any experimentation is necessary, but whether, *if experimentation is necessary, it is undue*." (emphasis added)

As directed by *In re Brana* and the MPEP at §2164.02, "Even with such evidence, the Examiner must weigh the evidence for and against correlation and decide whether one skilled in the art would accept the model as reasonably correlating to the condition. *In re Brana*, 51 F.3d 1560, 1566 (Fed. Cir. 1995)." Respectfully, in light of the discussion *supra* and the remarks previously presented, the evidence against accepting the model as reasonably correlating to the same efficacy in humans outweighs the evidence in favor of accepting the model as correlating to the same efficacy in humans. For these reasons, the rejection of 35 U.S.C. 112, first paragraph, is respectfully maintained.

Conclusion

Rejection of claims 1, 3-12 and 70 remains proper and is **maintained**.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Leslie A. Royds
Patent Examiner
Art Unit 1614

September 28, 2006

Ardin H. Marschel 9/29/06
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER